

AIDS TREATMENT UPDATE

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On and off

Doctors continue to warn patients: Beware the risks in stopping treatment

BY ANNA POPPA

As we reported in last month's New Year state-of-the-HAART review, a number of researchers are investigating the effects of taking a break from anti-HIV therapy. Like the new kid on the block struggling to fit in, this novel strategy has appeared in a variety of incarnations. Stop Go Therapy, Pulse Therapy, Cyclic Therapy – not forgetting the patients' favourite, Drug Holiday – have all been ditched in favour of Structured Treatment Interruptions, or STIs for short. The subtext to this latter variation isn't hard to miss – this is a serious name for a serious subject.

TREATMENT FATIGUE

Whilst HAART and the pursuit of the fully suppressed viral load has been seen as a life-long commitment, the realities of long-term therapy have presented a number of challenges to this maxim. Though experiences of treatment vary, for some people the rigours of contending with both pill schedules and persistent side-effects clearly count against the notion of non-stop therapy for life. After months or years on treatment, some people want time off, and may find the idea of a drug-free period particularly appealing when switching off a regimen which is failing.

ALTERING THE VIRAL PHENOTYPE

The use of 'Mega-HAART' regimens which include upwards of six or seven antiretrovirals by people who have previously taken most available treatment options, is another setting in which the possible role of treatment breaks are being explored. As we have previously reported in *AIDS Treatment Update* issue 79, a short period off drugs has been associated with

a shift in the viral population from one which is largely drug resistant to one which is largely drug sensitive (also called 'wild-type' virus). This shift to wild-type has been associated with an improved virological response once the Mega-HAART combination is begun, at least over the short-term. Whether taking a drug holiday or using a multi-drug combination offers more long-term benefit than alternative strategies is not known, because comparative studies have not taken place. Similarly, it's most likely that the shift to wild-type virus masks a minority population of resistant viruses, and there is no information to suggest that a break in treatment makes this resistant subset any more responsive to future treatment.

STIMULATING AN IMMUNE RESPONSE TO HIV

Reports from the enigmatic 'Berlin patient' have provided a third impetus. This man began HAART very soon after becoming infected, during the period known as primary infection, but because of adherence problems and other infections, took two breaks from treatment before stopping altogether. His viral load, which had been undetectable on treatment, rebounded with each treatment interruption, but to a progressively lower level. As long as two years off all

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anti-HIV drugs, his viral load has remained below 500 copies.

Several other research teams have since reported similar cases, (see *AIDS Treatment Update* issue 75). These have occurred in people treated during primary infection who had a series of treatment interruptions. It must be stressed, though, that for each success story there are many more failures – it seems the most common response to stopping drugs which were controlling HIV replication is that viral load will simply rebound.

So what might be going on? One theory is that the spikes in viral load which follow each treatment interruption prompt a containing response from the immune system which would not otherwise have been produced whilst viral replication was effectively ‘turned off’ by HAART. In the same way that the body responds to vaccinations, here the immune system learns to at least partially control HIV itself without the need for antiretrovirals.

Immunological reports from these cases provides some support for this theory. HIV-specific CD4 cells, considered to be one of the body’s key immune responses to HIV, are typically found in high quantities in the small subset of people who do not appear to experience disease progression or ill health despite many years of HIV infection, (often called long-term nonprogressors). These cells are also found at significant levels during primary infection, but appear to dwindle during chronic infection. Now several different research groups have reported, albeit in a limited number of people, that serial treatment interruptions are associated with a proliferation in HIV-specific CD4 cells.

Nobody is uncorking the champagne just yet though. Sceptics are quick to point out that our understanding of the role that HIV-specific immunity may have in controlling viral replication is not complete. For example, just how necessary or adequate HIV-specific CD4 cells are in delaying or halting disease progression has been a matter of debate amongst researchers. As Professor Tony Pinching of Bart’s Hospital, London, said, “We need to distinguish between what is a knee-jerk response from the immune system, rather than a meaningful, protective response”.

Similarly, it’s possible that the Berlin patient and the small number of cases like him may simply be long-term nonprogressors dressed up as STI-success stories; people who would always have gone on to maintain low viral load with or without the assistance of HAART.

NEW REPORTS IN PRIMARY INFECTION

In fact the number of cases reported so far is very small indeed. In addition to the Berlin patient¹, the US/Italian RIGHT Institute have

recently reported the experiences of three people who began treatment following seroconversion². During successive treatment interruptions, two of these maintained viral load below 5,000 copies for five and six months off therapy. However, despite five interruptions, the other patient did not maintain viral load suppression off HAART.

A further two people have been reported by New York’s Aaron Diamond Centre³, whose viral load remained undetectable for many months off therapy following several STIs. In the latter half of 1999, researchers from Brussels reported on a group of seven people treated during primary infection. Three of this number did not experience viral load rebound four to 24 months after stopping treatment⁴.

At November’s annual meeting of the Infectious Diseases Society of America, Rosenberg and colleagues from Boston reported two people who maintained viral load below 5,000 copies following either two or three STIs⁵. At the same meeting, doctors from Barcelona reported on a group of ten patients who began treatment early during infection and who are undergoing a series of STIs⁶. All began HAART with a CD4 count above 500 and with viral load between 30,000 and 50,000 copies. All had been taking protease inhibitor (PI)-containing HAART for at least eight months at the time of their first STI, and had maintained viral load below 20 copies throughout this period. Viral load rebounded in all cases at each interruption. However, of nine people who completed two STIs, viral load peaked and then fell to below 5,000 copies in four cases. All nine will now complete a third STI.

STIS IN CHRONIC INFECTION

Given that most people with HIV do not have their infection diagnosed as early as in the cases above, the impact of STIs in chronic infection is an important area of study. The US NoHRT study set up to investigate this has so far reported on sixteen chronically infected patients, who had been taking their PI-containing HAART regimen for at least two years on average⁷. Average CD4 count was high at around 900 cells, and the average time for which treatment had suppressed viral load below 500 copies was just over two years. On stopping treatment, most rebounded quickly, except for two outliers. One of these took seven weeks to experience viral load rebound, and the other – dubbed the Bethesda patient – maintained viral load below 500 copies some six months after stopping treatment.

At last Autumn’s European AIDS Conference in Lisbon, Lydia Ruiz reported on twelve chronically infected patients who agreed to

UK STUDY
A proposal for a trial evaluating both STIs and Mega-HAART in people with low CD4 counts who have previously taken all three drug classes is currently at the protocol stage. OPTIMA is under consideration by the UK Medical Research Council and the Canadian Trial Network.

stop their suppressive HAART therapy for a maximum of one month, or until viral load had risen above 3,000 copies⁸. All participants had maintained viral load below 20 copies for at least two years, and for 29 months on average. Average CD4 count was 1,202 cells. Once drugs were stopped, viral load rebounded in ten of the twelve, but the other two maintained suppression below 20 copies. On restarting, all suppressed viral load below 20 copies again.

Researchers from New York measured HIV-specific CD4 and CD8 responses in 22 chronically infected patients⁹. According to clinic records, eleven of these had a history of treatment interruptions, and it was in this group of patients that the broadest HIV-specific immune responses were seen.

A ROLE FOR IL-2?

One of last year's most intriguing studies came from researchers in New York, and investigated a year-long STI in a small group of chronically infected patients¹⁰. All had been previously treated with HAART plus a course of daily, low-dose injections of IL-2 (interleukin-2), taken for one year. Administration of IL-2 was continued throughout the period where HAART drugs were stopped.

In the nine people who have so far stopped HAART and continued with IL-2, viral load rebounded rapidly for an initial two weeks, before falling to a much lower level. The average peak viral load was around 350,000 copies, and fell to an average of 26,000 copies. Five of these patients have since chosen to restart HAART; the other four remain on IL-2 alone. No doubt this year's AIDS conferences will hear more from this group. For now, interpreting these results is difficult.

CAUTION: BE AWARE OF THE RISKS

The most common outcome for people who take an STI is that their viral load rebounds quickly as soon as drugs are stopped. Whilst it seems that restarting treatment will re-suppress viral replication, in the meantime there will be a loss of CD4 cells. The lower one's count at the time of the STI, the greater risk this will pose. In Veronica Miller's Mega-HAART cohort, where the multi-drug regimen was preceded by a break from treatment of at least two months, the average fall was 89 cells, from a pre-STI median of 155; a level which would itself place individuals at risk of opportunistic infections (OIs)¹¹. Though most people in this study regained their pre-STI CD4 count on the new regimen, many would consider this strategy too risky. At the very least, re-starting preventative treatments for OIs would be wise in these circumstances.

People who take an STI because of side-effects such as fatigue or diarrhoea may find their quality of life improves off drugs. This experience is not universal, however, and one effect of a rising viral load may be the production of unpleasant, flu-like symptoms anyway. Another outcome is that body tissues may be re-seeded with HIV, perhaps reversing some of the benefits gained by taking antiretrovirals in the first place. Immunological reports from NoHRT participants found that the reservoir of latently-infected, resting T-cells typically expanded in the period off drugs.

A further potential hazard is that stopping and starting regimens will result in drug resistance. There is little evidence that this occurs at present, but the risk may well be influenced by the particular drugs being taken. Some anti-HIV drugs, e.g. efavirenz, can still be found at low levels in the blood at least a week after the last dose was taken, whereas others may have disappeared in just a day or two. The use of STIs in people taking NNRTIs is even less well-studied than in people on PIs.

It is for these reasons that STIs are not recommended as a routine HIV treatment strategy at the moment. Each of the studies mentioned in this article provide intensive monitoring to participants during periods off treatment. Experimenting outside research settings, and particularly without the knowledge of your doctor, is unsafe. Very few people who have taken STIs have maintained control of their virus off drugs, compared to those whose viral load has rebounded, and there is no definitive proof that stopping treatment has been the cause of this control.

KEY CONCLUSIONS

- ♦ In theory, structured treatment interruptions, or STIs, may encourage the immune system to control HIV.
- ♦ In practice, most people who stop anti-HIV drugs have a rise in viral load and need to re-start treatment to reduce it.
- ♦ There are a few, very rare cases where viral load has remained low off treatment, including a few people who began treatment later in the course of infection. Immune responses to HIV seem to have expanded in these people.
- ♦ Stopping treatment may result in loss of the benefit gained, including a fall in CD4 count and increased risk of illness. The long-term implications are unknown, and so STIs are not recommended for general use at present.
- ♦ If you are having problems taking anti-HIV drugs, or are considering stopping treatment for any reason, discuss this with your doctor or another member of clinic staff.

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Anabolic steroids

Do they have a role in the treatment of wasting and weight loss?

BY ROBERT FIELDHOUSE

HIV-related wasting is defined as unintentional weight loss of 10% or more of normal body weight, in the absence of any infections, and is sometimes accompanied by persistent diarrhoea. The condition is potentially devastating since studies have shown a link between the loss of lean body mass (LBM) and decreased survival.

Weight loss can result from malabsorption of nutrients in food, diarrhoea, reduced intake of food and altered metabolism due to HIV infection. It is likely to be a concern for all positive people at some time or another. Oral thrush or other diseases affecting the mouth, like hairy oral leukoplakia or mouth ulcers can make it difficult to eat. Depression and anxiety can also suppress appetite.

Trials have suggested that beginning HAART may improve weight loss but that the weight gained after starting therapy may be in the form of fat^{1,2}. One small study found that some patients experienced a reduction in body weight after beginning HAART³.

It is important that the causes of weight loss be identified and appropriately treated. Consultation with your doctor or dietician will enable you to assess the quality of your diet and discuss any necessary adjustments, and this should happen at an early stage. It is generally recommended that a person with HIV-related weight loss should be using HAART. It is hoped that by strengthening the immune system, the body is better able to cope with opportunistic infections that may be contributing to the weight loss.

WHAT ARE ANABOLIC STEROIDS?

Anabolic steroids are synthetic versions of the male hormone testosterone, that promote the growth of skeletal muscle and increase lean body mass. Testosterone is produced both in the testicles and adrenal glands.

LOW TESTOSTERONE

Low testosterone is the most common hormone deficiency in HIV infection. It is estimated that around 40% of those with symptomatic illness have a deficiency. Low testosterone (hypogonadism) can result in decreased appetite, poorer metabolism of protein and carbohydrates, lowered mood, and decreased sexual function and sperm production. Decreased release of testosterone from the testes into the

bloodstream may be an effect of HIV infection of the testicular tissue or a result of the over-production of the stress hormone cortisol, which is common among individuals suffering from acute or chronic infections. This condition can also be caused by ketoconazole and ganciclovir, drugs used to treat OIs, as well as by cancer therapy, excessive marijuana use or synthetic testosterone therapy itself.

HOW ARE THEY TAKEN?

Steroids can be taken orally, by intramuscular injection, or can be absorbed through the skin. Safer injection practices should be used to avoid transmission of infections, and advice should be sought about avoiding bacterial infections. Skin patches and gel feed testosterone into the bloodstream through the skin of the trunk or the scrotum. In doing so they are less likely to shut down the body's natural production of testosterone.

Anabolic steroids deliver the best results if combined with a structured, resistance-training programme, specifically designed to stimulate muscle growth. Taken alone, the steroids themselves will not produce a beneficial effect. In addition, muscles require adequate nutrients. Without this the muscle will either tear or simply form stronger fibres without actually growing in size. You should increase intake of amino acids and protein rich food and use extra carbohydrates to fuel any activity. It is also advisable to increase vitamin and mineral intake.

SIDE-EFFECTS

The use of testosterone in HIV-positive people who have normal testosterone levels will produce no benefit. Instead it will merely shut down natural testosterone production. This will take several months to return to normal, and may cause symptoms such as lethargy and low mood on stopping the course.

If used in high doses, anabolic steroids are reported to have a number of serious side-effects. Some are more toxic to the liver than others and may produce unwanted effects such as acne, male pattern baldness, testicular shrinkage and impotence.

Only the steroids testosterone and oxandrolone have been studied to treat HIV-related wasting and hypogonadism, and even these are relatively poorly understood in terms of their long-term safety. Testosterone and

LIPODYSTROPHY

Body fat changes termed lipodystrophy are often seen among people using HAART, and needs to be distinguished from the more 'traditional' form of wasting seen in HIV disease. This may be difficult. It has been proposed that certain anti-HIV drugs may be responsible for fat loss. Others argue, however, that HAART-related lipodystrophy may also be due to the effects of HIV itself. It is as yet unclear what role anabolic steroids might play in the management of this syndrome. See aidsmap.com for more on this.

oxandrolone are used most often because they are considered to be less harsh on the liver and to have fewer side-effects.

All steroids can elevate liver enzymes, but levels usually return to normal once the cycle is stopped. Less common side-effects include stomach ache, insomnia, high blood pressure, enlarged prostate, which may cause difficulty with urination, and the development of female breasts (i.e. in men). Anabolic steroids also have the potential to alter mood, energy and appetite levels, and they may exacerbate aggressive tendencies. A possible safeguard may be to use them in cycles of six to eight weeks and then have a break, though side-effects should only be moderate if therapeutic dosing is not exceeded.

ARE STEROIDS IMMUNO-SUPPRESSIVE?

Proponents of the belief that steroids suppress the immune system have cited the argument that recreational users of the drugs often experience colds and flu-like symptoms after completing a cycle of steroids. However, therapeutic doses of these drugs are much lower than the doses taken by athletes. The only study to look at the effects of anabolic steroids on the immune systems of HIV-positive individuals showed no detrimental effect on CD4 or CD8 levels over the course of study.

CLINICAL STUDIES

Research into the therapeutic use of anabolic steroids for HIV-related wasting began in Australia in the early 1990's. Treatment with synthetic testosterone has been shown both in research and clinical practice to boost levels of the hormone in HIV-positive people. Data published in 1999 showed that testosterone remained safe and effective at increasing lean body mass (LBM) over the course of one year⁴.

Fifty-one HIV-positive men with low testosterone levels were enrolled in the study. The subjects received either 300 mg testosterone enanthate by intramuscular injection or placebo every three weeks for six months. After six months all participants received testosterone. Thirty-four men completed the study. Those receiving testosterone for twelve months gained approximately 3.4kg of LBM compared to 1kg in the group treated for only six months. Subjects who were switched from placebo to testosterone at six months began gaining LBM from this time point on. Few side-effects and no prostate damage were reported.

In March 1999, a study conducted in San Francisco reported a benefit when testosterone was combined with oxandrolone and resistance exercise⁵. Twenty-four HIV-positive men who had suffered involuntary weight loss

were randomly assigned to either 100mg testosterone by intramuscular injection once a week, and resistance training three times a week, or the same protocol and 20mg oral oxandrolone each day in addition. Improvements in energy and weight were observed in both groups by week eight but the weight gains among subjects in the oxandrolone group were significantly higher, 7kg as opposed to 4kg in the placebo arm. A sub-group of men who were also taking protease inhibitors were monitored and researchers concluded that the use of protease inhibitors did not affect gains in LBM or muscle strength. Mood swings were reported among five of the eleven men taking both testosterone and oxandrolone.

There has only been one study of the use of testosterone in HIV-positive women with wasting⁶. Weight increases were observed, though this was in the form of fat rather than LBM. No masculinisation was observed.

KEY CONCLUSIONS

- ◆ Weight loss is common and potentially dangerous among HIV-positive people. Testosterone levels should be checked for hypogonadism.
- ◆ The effects of low testosterone levels such as fatigue, low mood and loss of libido can be improved with testosterone replacement therapy. HRT can have the same effect among women.
- ◆ Testosterone therapy appears safe and effective for HIV-positive people with low testosterone levels, over the short-term, though this information has been gathered through studies involving relatively small numbers of people so far.
- ◆ There is no evidence that people with HIV with normal testosterone levels will benefit from additional testosterone.
- ◆ Anabolic steroids, whilst promoting significant gains in lean body mass, do not appear to suppress the immune system or cause severe side-effects, particularly when given in low doses, in cycles, and under medical supervision. Again, this information is based on relatively, small and short-term studies.
- ◆ Concomitant protease inhibitor therapy does not prevent improvement in lean body mass. It may be advisable to have liver enzymes and HDL cholesterol checked regularly, however.
- ◆ A multi-disciplinary approach incorporating low dose anabolic steroids with resistance training and appropriate advice regarding diet, carried out under medical supervision, should be considered by people affected by wasting, and discussed with your doctor.

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New trials open

A brief guide to clinical trials currently enrolling in the UK

BY ROBERT FIELDHOUSE

GROWTH HORMONE FOR WASTING

Human growth hormone (HGH) is a naturally occurring hormone involved in the production of protein in muscle cells, and the release of energy from fats. Study 9037 is a trial of the recombinant (genetically modified) version, designed to test the efficacy of rHGH (r for recombinant) to treat HIV-related wasting. Participants will be allocated at random into one of three groups, all of which will receive daily injections. Group one will receive rHGH every day. Group two will receive alternate injections of rHGH and placebo, and Group three will receive only placebo. Treatment is blinded, so neither you nor your doctor will know which group you are in.

The trial will last twelve weeks, and injections will be self-administered at home. Participants will be expected to attend the clinic eight times over a 28 week period. To participate you will need to be aged 18 or over, have evidence of HIV-related wasting and have been on antiretroviral treatment for at least eight weeks.

Exclusion criteria include the presence of an active opportunistic infection or a history of pancreatitis, glucose intolerance, coronary disease, carpal tunnel syndrome or any disorder associated with oedema (accumulation of fluid below the skin or in the cavities of the body). Pregnant and breast feeding women will also be excluded from participating in this study.

This trial is enrolling at sites 1, 2, 3, 4 and 11 (see sidebar to left).

TAXOL FOR KS

TAX/22-99.002 is a study designed to assess the efficacy and tolerability of *Taxol*, which is currently used as an anti-cancer drug in the USA, among people who have advanced KS and who have already received treatment for it. All participants will receive *Taxol*, which will be administered every fourteen days by an intravenous infusion which takes three hours. The treatment will continue for as long as clinical benefit is evident.

To be eligible for the study you will need to be aged 18 or over, have symptomatic KS, and have previously used at least one chemotherapy regimen given to treat KS. Exclusion criteria include prior exposure to *Taxol*, or being allergic to its components, or having any history of neoplasm (an abnormal

or uncontrolled growth of tissue), or cardiac disease. This trial is not open to pregnant or breast feeding women.

This trial is enrolling at sites 1, 3, 5, 6, 7 and 8 (see sidebar to left).

THE RESTART STUDY

This study is designed to determine if the nucleoside analogues d4T and ddI can be successfully recycled when all other treatment options have been exhausted. All participants will stop their current regimen and take d4T and ddI once daily for six weeks. At this point, viral load and resistance tests will be performed and hydroxyurea will be added. Six weeks later, an additional viral load and resistance test will be carried out and the combination will be completed by the addition of abacavir (another nucleoside analogue), and the PIs ritonavir and saquinavir.

To be eligible, you must be aged 18 or over, and have taken all of the following drugs for at least eight weeks: AZT, d4T, ddI, ddC and 3TC. Your viral load must be over 5,000 copies and your CD4 count must have fallen by more than 100 cells, or by 50%, in the previous six months.

This trial is enrolling at sites 3, 9 and 10 (see sidebar to left).

ABT-378 VERSUS PI

Early data on the protease inhibitor (PI) ABT-378 suggests that it is well tolerated and highly potent. This study, called protocol M98-888, is designed to compare the safety and antiviral activity of ABT-378, plus the NNRTI nevirapine, taken together with two nucleoside analogues, against a PI chosen by your doctor plus nevirapine and two new nucleoside analogues, in people who are antiretroviral experienced. All participants will know which PI they are taking, and will have to attend the clinic for regular monitoring.

To be eligible, you must be aged twelve or over, have a viral load of between 100 and 100,000 copies, and have previously taken a single PI and double nucleoside analogue containing regimen for at least twelve weeks. You will be excluded if you have been treated for an active opportunistic infection in the last 30 days. Pregnant and breast feeding women will also be excluded.

This trial is enrolling at sites 1, 3 and 6 (see sidebar to left).

TRIAL SITES KEY

1 Royal Sussex County Hospital, Brighton 01273 664532

2 Western General Hospital, Edinburgh 0131 536 6220

3 Chelsea and Westminster Hospital, London 020 8746 8000

4 St George's Hospital, London 020 8725 3355

5 Kings College Hospital, London 020 7346 3479

6 St Mary's Hospital, London 020 7725 6790

7 St Thomas' Hospital, London 020 7928 9292

8 The Middlesex Hospital, London 020 7636 8333

9 Charing Cross Hospital, London 020 8846 7582

10 Victoria Clinic for Sexual Health, London 020 8746 8066

11 Royal Free Hospital, London 020 7794 0500

Open-label ABT

The new protease inhibitor ABT-378 (lopinavir) is to be made available in the UK to people who have run out of other protease inhibitor options. Abbott Laboratories has established a study which will make ABT-378 available to anyone who has experienced treatment failure or intolerance to at least two protease inhibitors, provided their viral load is greater than 10,000 copies, and who has had a CD4 count below 200 in the past three months and/or an AIDS defining illness that has occurred since commencing HAART.

Individuals should not be taking any other drugs which interact negatively with ritonavir, since ABT-378 is encapsulated with a very small dose of ritonavir in order to boost blood levels of the new drug. Ritonavir interacts with a good many drugs, so seek advice from your doctor or HIV pharmacist on this question, not forgetting to mention over-the-counter medications. Pregnant women or those with liver function test values more than five times the upper limit of normal will not be permitted to receive ABT-378 for safety reasons.

At the time of going to press, the Royal Free Hospital had begun enrolling. The Chelsea and Westminster Hospital and the Mortimer Market Centre in London are also expected to take part in the study, along with the North Manchester Hospital. Abbott Laboratories is currently seeking permission from the Medicines Control Agency to expand the study to other hospitals in the UK. Clinicians interested in participating should contact the Clinical Research Department at Abbott. More information about the potential use of ABT-378 in salvage therapy can be found on aidsmap.com.

Hep C & HAART

Although people with hepatitis C have a four-fold higher risk of developing liver toxicity on HAART, almost 90% do not suffer any significant liver problems as a result of their anti-HIV treatment, according to a study in the January 5th issue of the *Journal of the American Medical Association*. The findings challenge the view that protease inhibitors are especially difficult to tolerate if you are co-infected with hepatitis C.

However, the study also confirms the view that ritonavir is responsible for a much higher rate of liver toxicity among all patients,

regardless of co-infection with hepatitis C. Amongst a group of 300 people, two thirds of whom had received protease inhibitors, and half of whom had hepatitis C, one in ten developed serious liver toxicity. Ritonavir accounted for half of these cases though the drug was taken by only 50 patients. Manufacturers Abbott Labs point out that this rate is higher than that seen in clinical trials.

New test

A report in the January 2000 edition of *Nature Medicine* describes a new test which can be used to detect ongoing, low-level HIV replication in people who receive an undetectable result using more standard viral load tests. The new technique looks for looped portions of HIV DNA, called LTR circles. These are formed when viral enzymes are inserted into DNA in immune cells, a step in HIV's reproductive process. However, the test is used in very limited research settings at present and is a long way from use in routine patient care.

BHIVA guidelines

Updated recommendations on the use of anti-HIV therapy in adults from the British HIV Association are now available on the NAM/BHIVA website aidsmap.com. As usual, to reach [aidsmap](http://aidsmap.com), point your browser to <http://www.aidsmap.com>.

New from NAM

The first booklet in NAM's information series for positive people, *Viral Load*, has recently been fully revised to take account of new guidelines on the management of anti-HIV therapy from the British HIV Association. This second edition offers a plain English guide to viral load testing both for those on treatment, and for those who are not taking HIV drugs.

People personally affected by HIV can order free copies of this booklet, and others in the series, by writing, telephoning or emailing NAM (see contact details on back page). Organisations can buy copies at 50p each – simply send remittance and a covering note to NAM (cheques payable to NAM Publications).

The other titles in this series are *Anti-HIV Drugs*, *Resistance*, *Clinical Trials* and *Nutrition*. A sixth will be added very soon, a *Glossary* of medical terms which we'll be sending to all *AIDS Treatment Update* readers.

NAM FORUM

The next NAM Information Forum is on Monday, February 28th and will provide feedback from the 7th Retroviruses Conference, a key HIV medical meeting happening in San Francisco in early February. The venue is the Palms Room, 4th Floor, University of London Union, Malet Street, London WC1. Forums are free and run from 7pm to 9pm, and a sign language interpreter is available.

GLOSSARY OF TERMS

antiretroviral Something that attacks retroviruses such as HIV

CD4 Molecule on the surface of some cells onto which HIV binds. CD4 cell count roughly reflects the state of the immune system

CD8 Molecule on the surface of some white blood cells. Some of these cells can kill other cells which are infected with foreign organisms

clinical outcome The occurrence of a physical symptom

cross resistance When resistance to one drug reduces the virological response to subsequent treatment with another drug which has not been taken before

expanded access scheme A programme which allows access to an experimental drug outside clinical trials for people in need

interleukin-2 A chemical which stimulates the immune system

lipid A general term for fats in the blood

log Short for logarithm, a measurement scale often used when describing viral load

nadir The lowest point to which viral load falls after starting anti-HIV drugs

NNRTI Non-nucleoside reverse transcriptase inhibitors: anti-HIV drugs that include nevirapine, delavirdine, and efavirenz

NRTI Nucleoside analogue reverse

transcriptase inhibitors: anti-HIV drugs that include AZT, ddI, ddC, 3TC and d4T

phenotype Trait or behaviour which results from a particular genetic code

protease An enzyme that HIV uses to break up large viral proteins into smaller ones

protease inhibitor Anti-HIV drugs which target the protease enzyme, e.g. saquinavir, ritonavir, indinavir, nelfinavir

recombinant regimen Drug or treatment combination

resistance A drug-resistant HIV strain is less susceptible to the effects of one or more anti-HIV drugs because of its genetic make-up

reverse transcriptase An enzyme which converts genetic material from RNA into DNA, an essential step in the lifecycle of HIV

steroids Immune-suppressing drugs used to damp down excessive immune responses

undetectable viral load A level of viral load that is too low to be picked up by the particular viral load test used

viral load The amount of virus in a sample. HIV viral load indicates the rate at which HIV is reproducing in the body

virologic response Effect of treatment on viral load

wild-type virus Virus which has not been exposed to anti-HIV drugs before

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16a Clapham Common
Southside
London SW4 7AB.
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Fax: 020 7627 3101
Email: atu@nam.org.uk

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Editor:
Anna Poppa

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ANY QUESTIONS?

The following national agencies, all based in London, offer one-to-one advice and information about treatment options, in person or over the telephone:

◆ AIDS Treatment Project

Phoneline: 0845 9470047
Mon & Wed 3pm - 9pm, Tue 3pm - 6pm
All calls charged at local rates.

◆ Body Positive

Treatment Advice: Tue & Wed 12pm - 5.30pm
Call Anthony on 020 7287 8010 to make an appointment.

◆ The Terrence Higgins Trust

Helpline: 020 7242 1010 Daily 12noon - 10pm
Treatment Support: Call the Treatments Team on 020 7831 0330 for an appointment.

NAM recommends readers to seek treatment advice from more than one source, and to discuss all your decisions with your doctor.

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